

AMENDMENTS TO THE CLAIMS

1. (Withdrawn-Currently Amended) ~~Use of a virus, preferably~~A method for the treatment of a tumor comprising administering an adenovirus to a subject suffering from the tumor, wherein the cells forming the tumor or part thereof have YB-1 in the nucleus and~~for the manufacture of a medicament, characterised in that~~wherein the adenovirus is replication deficient in cells which lack YB-1 in the nucleus, and whereby the adenovirus encodes an oncogene or oncogene product, in particular an oncogene protein, E1A which transactivates at least one viral gene, preferably an adenoviral gene, whereby the adenoviral gene is selected from the group comprising E1B55kDa, E4orf6, E4orf3 and E3ADP.

2. (Canceled)

3. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 or 2~~claim 1, characterised in that ~~the virus, preferably~~ the adenovirus[[,]] replicates in cells which have YB-1 in the nucleus.

4. (Canceled)

5. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~claim 4~~claim 1, characterised in that the ~~viral oncogene protein~~ E1A is capable of binding a functional Rb tumor suppressor gene product.

6. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~claim 4~~claim 1, characterised in that the ~~viral oncogene protein~~ E1A is incapable of binding a functional Rb tumor suppressor gene product.

7. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 4 to 6~~claim 1, characterised in that the ~~viral oncoprotein~~ E1A does not induce nucleus localisation of YB-1.

8. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 or 3 to 7~~claim 1, characterised in that the ~~medicament is for~~ patients whose cells of the patient are Rb positive or Rb negative.

9. (Withdrawn-Currently Amended) ~~Use~~The method according to claim 8, characterised in that the cells are those cells which are involved in the formation of the ~~condition~~tumor ~~which is to be influenced by the medicament.~~

10. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 to 9~~claim 1, characterised in that the cells are Rb negative and the cell nucleus is YB-1 positive, preferably YB-1 positive in the nucleus independent from the cell cycle.

11. (Canceled)

12. (Withdrawn-Currently Amended) ~~Use~~The method according to claim 11, characterised in that the cells, preferably the cells forming the tumor or parts thereof, are resistant, preferably multiple resistant against pharmacological agents, preferably anti-tumor agents and more preferably cytostatics.

13. (Withdrawn-Currently Amended) ~~Use~~The method according to claim 12, characterised in that the cells express, preferably overexpress ~~of~~ the membrane-anchored transport protein P glycoprotein.

14. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 to 13~~claim 1, characterised in that the cells are p53 positive or p53 negative.

15. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 5 or 7 to 14~~claim 1, characterised in that the ~~oncogene protein~~E1A exhibits one or several mutations or deletions compared to the wildtype oncogene protein E1A, whereby the deletion is preferably one selected from the group ~~comprising~~consisting of deletions of the CR3 region and deletions of the N-terminus and deletions of the C-terminus.

16. (Withdrawn-Currently Amended) ~~Use~~The method according to claim 15, characterised in that the E1A oncogene protein is capable of binding to Rb.

17. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 6 to 14~~claim 1, characterised in that the ~~oncogene protein~~E1A comprises one or several mutations or deletions compared to the wildtype oncogene protein, whereby the deletion is preferably a deletion in the CR1 region and/or CR2 region.

18. (Withdrawn-Currently Amended) ~~Use~~The method according to claim 17, characterised in that the oncogene protein E1A is incapable of binding to Rb.

19. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 to 18~~claim 1, characterised in that the ~~viral oncogene protein, preferably E1A~~[[,]] is under the control of a tissue and/or tumor specific promoter.

20. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 to 19~~claim 1, characterised in that ~~the virus, particularly the adenovirus~~[[,]] codes for YB- 1.

21. (Withdrawn-Currently Amended) ~~Use~~The method according to claim 20, characterised in that YB- 1 is under the control of a tissue specific and/or tumor specific promoter.

22. (Withdrawn-Currently Amended) ~~Use~~The method according to ~~any of claims 1 to 21~~claim 1, characterised in that the ~~virus, preferably the adenovirus~~, codes for at least one protein,

whereby the protein is selected from the group ~~comprising~~ consisting of E4orf6, E4orf3, E1B55k and adenoviral E3ADP protein.

23. (Canceled)

24. (Withdrawn-Currently Amended) ~~Use~~ The method according to ~~any of claims 1 to 23~~ claim 1, characterised in that the tumor comprises YB-1 in the nucleus after induction of the transport of YB-1 into the nucleus.

25. (Withdrawn-Currently Amended) ~~Use~~ The method according to claim 24, characterised in that the transport of YB-1 is triggered by at least one measure selected from the group ~~comprising~~ consisting of irradiation, administration of cytostatics and hyperthermia.

26. (Withdrawn-Currently Amended) ~~Use~~ The method according to claim 25, characterised in that the measure is applied to a cell, an organ or an organism.

27. (Withdrawn-Currently Amended) ~~Use~~ The method according to ~~any of claims 1 to 26~~ claim 1, characterised in that the ~~virus, preferably the adenovirus~~ [[,]] is selected from the group ~~comprising~~ consisting of AdΔA24, dl1922-947, ElAd/01/07, dl1119/1131, CB 016, dl520 and viruses lacking an expressed viral oncogene which is capable of binding a functional Rb tumor suppressor gene product.

28. (Canceled)

29. (Canceled)

30. (Currently Amended) An isolated adenovirus comprising a viral oncogene protein, wherein the viral oncogene protein is E1A and ~~Viral oncogene protein, preferably an isolated viral oncogene protein, characterised in that it comprises the following characteristics:~~

- (a) ~~transactivation of~~ it mediates transactivation of at least one viral gene, whereby the viral gene is selected from the group ~~comprising~~ consisting of E1B-55k, E3ADP and E4orf6 and E4orf3; and
- (b) ~~lack of induction of~~ it does not induce YB-1 activity in a nucleus, preferably in the nucleus of the cell, in which the viral oncogene protein is present, wherein the adenovirus is replication deficient in cells which lack YB-1 in the nucleus but replicates in cells which have YB-1 in the nucleus.

31. (Canceled)

32. (Currently Amended) ~~Viral oncogene protein~~ The adenovirus according to claim 30 ~~or 31~~, characterised in that the viral oncogene protein E1A comprises one or several mutations or deletions ~~compared to the wildtype oncogene protein~~, whereby the deletion is ~~preferably selected~~

~~from the group comprising deletion of the CR3 region, deletion of the N-terminus and deletion of the C-terminus within a CR3 region, a N-terminus region, a C-terminus region, or combination thereof of the E1A oncogene protein.~~

33. (Currently Amended) ~~Viral oncogene protein~~ The adenovirus according to claim 32, characterised in that ~~it~~ the viral oncogene protein E1A is capable of binding to Rb.

34. (Currently Amended) ~~Viral oncogene protein~~ The adenovirus according to claim 30 ~~or 34~~, characterised in that the viral oncogene protein E1A comprises one or several mutations or deletions, whereby the deletion is preferably a deletion in the CR1 region and/or the CR2 region of the E1A oncogene protein.

35. (Currently Amended) ~~Viral oncogene protein~~ The adenovirus according to claim 34, characterised in that the viral oncogene protein is incapable of binding to Rb.

36. - 38 (Canceled)

39. (Withdrawn-Currently Amended) ~~Use~~ The method according to claim 38, characterised in that the cells, ~~preferably the cells forming the tumor or parts thereof, have a resistance, preferably a multiple resistance against pharmacologically active agents, preferably anti-tumor agents and more preferably cytostatics.~~

40. - 46 (Canceled)

47. (Withdrawn-Currently Amended) ~~Use of a virus, preferably an adenovirus, according to any of claims 1 to 29~~ The method according to claim 1, whereby wherein the adenovirus comprises a nucleic acid coding for a transgene.

48. (Withdrawn-Currently Amended) ~~Use of a virus, preferably an adenovirus,~~ The method according to ~~any of claims 1 to 29~~ claim 1, whereby wherein the adenovirus comprises the translation and/or transcription product of a transgene.

49. (Canceled)

50. (Canceled)

51. (Withdrawn-Currently Amended) ~~Use~~ The method according to ~~any of claims claim 47 to 50, whereby wherein~~ the transgene is selected from the group ~~comprising consisting of~~ prodrug genes, cytokines, apoptosis-inducing genes, tumor suppressor genes, genes for metalloproteinase inhibitors and genes for angiogenesis inhibitors.

52. (Withdrawn-Currently Amended) ~~Use~~ The method according to ~~any of claims 47 to 50~~ claim 47, whereby wherein the transgene is selected from the group ~~comprising consisting of~~

nucleic acids for siRNA, for aptamers, for antisense molecules and/or ribozymes, whereby the siRNA, the aptamer, the antisense molecule and/or the ribozyme are targeting a target molecule.

53. (Withdrawn-Currently Amended) ~~Use The method~~ according to claim 52, ~~whereby~~ wherein the target molecule is selected from the group ~~comprising~~ consisting of resistance relevant factors, anti-apoptosis factors, oncogenes, angiogenesis factors, DNA synthesis enzymes, DNA repair enzymes, growth factors, receptors for growth factors, transcription factors, metalloproteinases, preferably matrix metalloprotein kinases, and plasminogen activator of the urokinase type.

54. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of the preceding claims~~ claim 1, ~~whereby~~ wherein the ~~medicament method~~ further comprises administering a pharmaceutically active compound.

55. (Withdrawn-Currently Amended) ~~Use The method~~ according to claim 54, ~~whereby~~ wherein the pharmaceutically active compound is selected from the group ~~comprising~~ consisting of cytokines, metalloproteinase inhibitors, angiogenesis inhibitors, cytostatics, cell cycle inhibitors, proteasome inhibitors, recombinant antibodies, inhibitors to the signal transduction cascade and protein kinase.

56. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of the preceding claims~~ claim 54, characterized in that the ~~medicament method~~ comprises administering a combination of at least two agents, whereby each and any of the agent is individually and independently selected from the group ~~comprising~~ consisting of cytostatics.

57. (Withdrawn-Currently Amended) ~~Use The method~~ according to claim 56, characterized in that at least two of the agents address different target molecules.

58. (Withdrawn-Currently Amended) ~~Use The method~~ according to claim 57, characterized in that at least two of the agents act through a different mode of action.

59. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of claims 56 to 58~~ claim 56, characterized in that at least one agent increases the capacity of a cell to be infected in which the virus replicates.

60. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of claims 56 to 59~~ claim 56, characterized in that at least one agent influences the availability of a component of the cell, preferably increases the availability of their component, whereby the component mediates the uptake of the virus.

61. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of claims 56 to 60~~ claim 56, characterized in that at least one agent mediates the transport of YB-1 into the nucleus, preferably increases said transport.

62. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of claims 56 to 64~~ claim 56, characterized in that at least one agent is a histone deacetylase inhibitor.

63. (Withdrawn-Currently Amended) ~~Use The method~~ according to claim 62, characterized in that the histone deacetylase inhibitor is selected from the group ~~comprising~~ consisting of Trichostatin A, FR 901228, MS-27-275, NVP-LAQ824, PXD101 Apicidin and Scriptaid.

64. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of claims 56 to 62~~ claim 56, characterized in that at least one agent is selected from the group ~~comprising~~ consisting of Trichostatin A, FR 901228, MS-27-275, NVP-LAQ824, PXD101 Apicidin and Scriptaid.

65. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of claims 56 to 64~~ claim 56, characterized in that at least one agent is a topoisomerase inhibitor.

66. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~claims~~ claim 65, characterized in that the topoisomerase inhibitor is selected from the group ~~comprising~~ consisting of Camptothecin, Irinotecan, Topotecan, DX-8951f, SN-38, 9-aminocamptothecin, 9-nitrocamptothecin, Daunorubicin and Etoposid.

67. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of the preceding claims~~ claim 55, characterized in that the agent comprises Trichostatin A and Irinotecan.

68. (Withdrawn-Currently Amended) ~~Use The method~~ according to ~~any of the preceding claims~~ claim 56, characterized in that the adenovirus, ~~in particular the virus according to any of the preceding claims~~, is separated from the at least two agents.

69. (Withdrawn-Currently Amended) ~~Use The method~~ according to claim 68, characterized in that at least one unit dosis of the virus is separated from at least one unit dosis of one or the at least two agents.

70. (Canceled)